UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,538	12/21/2000	David Aaron Katz	6652.US.01	2085

23492 7590 03/21/2006

ROBERT DEBERARDINE
ABBOTT LABORATORIES
100 ABBOTT PARK ROAD
DEPT. 377/AP6A
ABBOTT PARK, IL 60064-6008

EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/747,538	KATZ ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,18,38-41 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,18,38-41 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 13, 2006 has been entered.

Status of the Application

2. The action is in response to the RCE filed on January 13, 2006. Currently claims 17-18, 38-41, 43 are pending. Claims 17 and 38 are amended. Claims 1-16, 19-37, and 42 are cancelled. All arguments and amendment have been fully considered and thoroughly reviewed and deemed persuasive in view of the amendment.

Priority

3. This application is filed on December 21, 2000 claims benefit of US provisional application 60/173,699 filed on 12/30/1999.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 provides for the use of amplification conditions of claim 17, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. That is it is not clear whether the instant claim utilizes the thermal cycle conditions or four cycle steps of claim 17 or does it utilize a probe and the four thermal cycle steps of claim 17. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 41 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38-40, 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Evans et al. (J Clin Invest., Vol. 91, pp. 2150-2154, 1993).

Evans et al. teach a method of claim 38, for detecting a target nucleic acid sequence suspected of having a single or larger deletion or insertion in a test sample comprising

(a) contacting the test sample with amplification reagents comprising amplification primer (see page 2151, col. 1, paragraphs 1-2);

(b) subjecting the reaction mixture to amplification conditions to form a target nucleic acid sequence amplification product (See page 2151, col. 1, paragraph 2);

(c and d) detecting a first and second signal corresponding to a deletion and a standard nucleic acid (wild type amplification product) (see page 2151, col. 2, Fig. 1, paragraph 1);

(e) comparing the first and second signals to determine a deletion or insertion of at least 50 base pairs is present in the DNA in the test sample (see Fig. 1), wherein the amplification reagents comprise one primer that hybridizes to both the target and the standard nucleic acid sequence (see page 2151, col. 1, paragraph 2 indicating primer A2 in the amplification reagent that hybridizes to both target deletion and wild-type nucleic acid sequence).

With regard to claim 39-40, Evans et al. teach that the deletion is of 11.5kb (which includes the limitation of claims 39-40) (see page 2151, col. 1, paragraph 2-3, Fig.1);

With regard to claim 43, Evans et al. teach that the deletion is in the CYP2D6 locus, which is a polymorphic (see page 2151, col. 1, paragraph 2-3, Fig.1). Accordingly the instant claims are anticipated by Evans et al.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al. (J Clin. Invest., Vol. 91, pp. 2150-2154, 1993) in view of Van Ness et al. (USPN. 6,361,940).

Evans et al. teach a method for detecting a target nucleic acid sequence suspected of having a single or larger deletion or insertion in a test sample comprising

(a) contacting the test sample with amplification reagents comprising amplification primer (see page 2151, col. 1, paragraphs 1-2);

(b) subjecting the reaction mixture to amplification conditions to form a target nucleic acid sequence amplification product (See page 2151, col. 1, paragraph 2);

(c and d) detecting a first and second signal corresponding to a deletion and a standard nucleic acid (wild type amplification product) (see page 2151, col. 2, Fig. 1, paragraph 1);

(e) comparing the first and second signals to determine a deletion or insertion of at least 50 base pairs is present in the DNA in the test sample (see Fig. 1), wherein the amplification reagents comprise one primer that hybridizes to both the target and the standard nucleic acid sequence (see page 2151, col. 1, paragraph 2 indicating primer A2 in the amplification reagent that hybridizes to both target deletion and wild-type nucleic acid sequence). Evans also teach that the target is a polymorphic nucleic acid sequence (CYP2D6 locus) (see page 2151, col. 1, paragraph 2-3, Fig.1).

However Evan et al. did not specifically teach amplification temperature cycles of claim 17.

Van Ness et al. teach a method for detecting a target nucleic acid sequence (CYP2D6) in a test sample comprising PCR thermal cycling conditions comprising (i) maintaining the reaction temperature for a time and at temperature above 90 C sufficient to dissociate double stranded nucleic acid sequences (denaturation at 94 C for 30 sec), maintaining reaction mixture for a time and at a temperature from 45 to 65 C to allow primers to hybridize to the target nucleic acid (annealing temperature 62 C for 30 sec), (iii) maintaining the reaction mixture for a time and at a temperature at least above the temperature in (ii) (68 C for 4 min +20 sec/cycle) (iv) raising the temperature of the reaction mixture to a temperature sufficient to activate the polymerase (68 C for 10 min) and repeatedly performing cycles to form an amplification product (repeated for 20 cycles) (see col. 98, line 55-65).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine the method of amplification of a target nucleic acid as taught by Evans et al. with the step of PCR amplification cycles as taught by Van Ness et al. to achieve expected advantage of developing a sensitive and enhanced method for amplification of a specific target. An ordinary skill in the art would have reasonable expectation of success that the modification of the method taught by Evans with the thermal cycle steps taught by Van Ness et al. would result in identification of both wild-type and mutant alleles in the target nucleic acid (see col. 97, line 34-67, col. 98, line 1-67) Therefore an ordinary practitioner would have been motivated to combine the method of Evans et al. with the inclusion

of thermal cycles as taught by Van Ness et al. to develop a sensitive and enhanced method for identifying both wild- type and mutant alleles in a single reaction.

B. Claim 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al. (J Clin Invest., Vol. 91, pp. 2150-2154, 1993) in view of Van Ness et al. (USPN. 6,361,940) as applied to claim 41 above, and further in view of Wittwer et al. (USPN. 6,232,079).

Evans et al. in view of Van Ness et al. teach a method for detecting a target nucleic acid sequence suspected of having a single or large deletion or insertion as discussed above in section 6A.

Neither Evans et al. nor Van Ness et al. teach use of a probe in amplification reaction.

Wittwer et al. teach a method for monitoring hybridization during PCR (real-time PCR) for detecting a target nucleic acid sequence in a test sample comprising (a) contacting the test sample with amplification reagents comprising a polymerase, a PCR primer pair, and a probe (see column 6, lines 1-15, column 44, lines 24-38); (b) performing PCR cycles (i) raising temperature to dissociate the double-stranded genomic DNA, lowering the temperature to allow primers and probe to hybridize to the target nucleic acid, raising the temperature to dissociate the target-probe hybrids and extending the primers and continuously raising the temperature to temperature dependent polymerase extension (see column 44, lines 50-67, column 45, lines 1-12); (c) repeatedly performing the PCR cycles to form an amplification product (see column 45, lines 13-53) and (d) detection of the amplification product as an indication of presence of the nucleic acid (see column 45, lines 13-53).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine the method of amplification of a target

nucleic acid as taught by Evans et al. in view of Van Ness et al. with the step of primer extension in the presence of a probe or monitoring hybridization during PCR as taught by Wittwer et al. to achieve expected advantage of developing a sensitive and enhanced method for amplification of a specific target. An ordinary skill in the art would have reasonable expectation of success that the modification of the method taught by Evans et al. in view of Van Ness et al. with the step of monitoring hybridization during PCR would result in continuously monitoring of DNA amplification, identification and quantitation of the target nucleic acid and reducing laborious processing steps after PCR to identify the said target nucleic acid (see col. 3, line 14-33 of Wittwer et al. patent). Therefore an ordinary practitioner would have been motivated to combine the method of Evans et al. in view of Van Ness et al. with the inclusion of step of monitoring hybridization during PCR as taught by Wittwer et al. to develop a sensitive and enhanced method for amplification and quantitation of a specific target nucleic acid.

Response to arguments:

7. With regard to the rejection of claims 17-18 under 35 USC 102(e) as being anticipated by Wittwer et al., Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein, in view of the amendment and the declaration under 37 CFR 1.132.

8. The Declaration submitted under 37 CFR section 1.132 is fully considered and the rejection under 35 USC 102(e) is withdrawn in view of the amendment and declaration.

9. With regard to the rejection of claims 38-40, 43 under 35 USC 102(b) as being anticipated by Meyer et al., Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein, in view of the amendment and new grounds of rejections.

10. With regard to the rejection of claims 41 under 35 USC 103(a) as being obvious over Meyer et al. in view of Wittwer et al., Applicants' arguments and amendment are fully considered and the rejection is withdrawn herein, in view of the amendment and new grounds of rejections.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Examiner
Art Unit 1637

Prabha Chunduru 3/16/07
SURYAPRABHA CHUNDURU
PATENT EXAMINER